

## Patient preferences for outcomes in clinical trials: implications for medicines optimization

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### Trials

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**O16****Improving the testing of treatment effect in clinical trials with time to event outcomes**Song Yang<sup>1</sup>, Ross Prentice<sup>1</sup>National Heart, Lung, and Blood Institute, NIH; <sup>2</sup>Fred Hutchinson Cancer Research Center**Correspondence:** Song Yang

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This abstract is not included here as it has already been published.

**O17****Value-added use of clinical study data: a biolinc perspective on creating well-annotated data packages for the wider scientific community**Leslie Carroll<sup>1</sup>, John Adams<sup>1</sup>, Corey Del Vecchio<sup>1</sup>, Karen Mittu<sup>1</sup>, Kevin Zhou<sup>1</sup>, Jane Wang<sup>1</sup>, Carol Giffen<sup>1</sup>, Elizabeth Wagner<sup>2</sup>, Sean Coady<sup>3</sup><sup>1</sup>Information Management Services, Inc.; <sup>2</sup>Translational Blood Science and Resources Branch, Division of Blood Diseases and Resources, National Heart, Lung, and Blood Institute; <sup>3</sup>Epidemiology Branch, Prevention and Population Sciences Program, Division of Cardiovascular Sciences, National Heart, Lung, and Blood Institute**Correspondence:** Leslie Carroll

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**Introduction**

The National Heart, Lung, and Blood Institute (NHLBI) established the Biologic Specimen and Data Repositories Information Coordinating Center (BioLINCC) [www.biolinc.nhlbi.nih.gov](http://www.biolinc.nhlbi.nih.gov) in 2008 to provide online access to NHLBI data and biospecimen resources. To assist non-study investigators' use of the datasets, each study's BioLINCC webpage provides information on the study design and results, including documents that provide insight into the study data. Given the recent interest by journal editors in the rapid release of publication data, the need for efficient curation methods is becoming more important. The procedures that have been developed by BioLINCC to review and prepare study datasets and documents for sharing with secondary users are one example of how this can be accomplished.

**Methods**

Data packages submitted to BioLINCC undergo review for secondary usability. Data dictionaries are examined for ease of use by researchers outside of the original study group. Reviews are performed to find any data elements that are considered personally identifiable information (PII) which are then redacted or recoded in order to de-identify the data for distribution. An informed consent questionnaire is completed to discern if there are any restrictions related to wide data sharing. A comparison of the data with a publication representative of the study as a whole, such as a primary outcome manuscript, is conducted. The population included in the analysis as well as key statistics are reproduced and deviations identified. Key variables used in the analysis (e.g. inclusion criteria, adjudicated variables, outcomes) are noted and the documentation is examined to ensure these variables are well annotated. If study biospecimens are being transferred to the NHLBI Biorepository, the link between clinical data and those specimens is verified. Additional documentation including the study protocol, informed consent templates, MOP/MOOs, annotated forms, codebooks, and a publications list are collected to provide a useful context for the data and biospecimens.

**Results**

Over the first seven years of BioLINCC, data from 139 completed studies were made available through BioLINCC and 666 requests for 1496 data packages were fulfilled. A total of 130 original data packages and updates were processed and shared with an average effort of 75 hours per data package. The level of effort varied, not according to the complexity of the study design, but due to the stage of curation of the submitted data and documentation. Additional effort at both BioLINCC and the parent study's coordinating center was required in nearly all reviews to prepare and obtain missing information such as algorithms for calculated analysis variables, explanatory data labels, code books, key

variables used in analyses, annotated forms, and biospecimen linking files. To date, over 600 publications are known to have resulted from requestors using BioLINCC resources.

**Conclusion**

Efficient preparation of study data and documents is essential to maximizing the scientific utility of study resources. Preparing data for release to the general scientific community requires a significant commitment of time and effort to ensure investigators, not affiliated with the original study, have sufficient information to effectively conduct secondary analyses.

**O18****Patient preferences for outcomes in clinical trials: implications for medicines optimization**Emily Holmes<sup>1</sup>, Anthony G. Marson<sup>2</sup>, Dyfrig A. Hughes<sup>1</sup><sup>1</sup>Bangor University; <sup>2</sup>University of Liverpool**Correspondence:** Emily Holmes

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**Background**

Drug choices for given therapeutic indications are often guided by clinical trial evidence, however, patients may consider outcomes beyond those measured as primary endpoints within trials in their decision to adhere to medication. Discrete choice experiments (DCEs) are a valid method that has been used to quantify patient preferences for drug outcomes. Data from DCEs may be combined with the results of clinical trials to provide a more patient-orientated perspective on drug choice.

**Objective**

To demonstrate the impact of incorporating patients' benefit-risk preferences into the results of clinical trials, using a case study of preferences for anti-epileptic drugs (AEDs).

**Methods**

Preference weights for outcomes of AEDs (12-month remission, fewer seizures, depression, memory problems, aggression, foetal abnormality) were derived from a web-based DCEs of 414 adult patients with epilepsy. Rates for each of these outcomes were extracted from a large randomised controlled trial comparing the effectiveness of new and standard AEDs (SANAD), and from a systematic review of treatments of epilepsy in pregnancy. The preference weights were combined with the clinical event rates to estimate of patient utility for each AED. The probability of patients preferring each AED was then calculated as the ratio of exponentiation of the utility of each individual AED to the sum of the exponentiation of the utilities of all AEDs. Results were compared to rankings of AEDs as indicated by clinical trials.

**Results**

The rank order of AEDs based on trial data for remission: lamotrigine, carbamazepine, topiramate, oxcarbazepine, then gabapentin, changed when patient benefit-risk preference was considered. The probability of patients with partial epilepsy preferring each AEDs was, in descending order: carbamazepine (0.29), lamotrigine (0.26), oxcarbazepine (0.24), gabapentin (0.15), topiramate (0.07). Women with the potential to become pregnant, had a preference probability of: lamotrigine (0.31), oxcarbazepine (0.21), gabapentin (0.20), carbamazepine (0.19), topiramate (0.09). Comparable results were found for patients with generalised or unclassified epilepsy. Changes to rank ordering are explained by patients' stronger preferences for reducing the risk of AEs than for improving treatment benefit. In return for a 1% improvement in 12-month remission, the maximum acceptable risk of adverse events was: depression 0.31%, memory problems 0.30%, aggression 0.25%. The maximum acceptable risk of adverse event in exchange for a 1% improvement in 12-remission was, for women with the potential to become pregnant was: depression 0.56%, memory problems 0.34%, and foetal abnormality 0.20%.

**Conclusions**

DCEs represent a robust method for quantifying benefit-risk preferences that can be analysed alongside clinical trial data, to provide a patient-orientated perspective on the optimal choice of treatment.